ANNUAL REPORT

OF

THE HOWE LABORATORY OF OPHTHALMOLOGY

HARVARD MEDICAL SCHOOL

1955

243 CHARLES STREET

BOSTON, MASSACHUSETTS

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ALMOST critical event in the physical life of the Howe Laboratory is about to occur as this Report is being written, for the Laboratory is soon to have new quarters. It will occupy one of the three floors that comprise the new research facilities of the Eye and Ear Infirmary. The new quarters will permit some expansion in space (approximately 800 square feet more than the present 3700 square feet) and considerably more efficient operation.

Such a major step inevitably evokes a look-back at the past and a forecast for the future, and particularly an evaluation of our relationship, as a division of the Harvard Medical School, to the Massachusetts Eye and Ear Infirmary which houses us. The Howe Laboratory has been situated at the Infirmary for about a quarter of a century, almost its entire existence. It was the first substantially endowed laboratory for eye research in this country and has been a pioneer in clinical research on the eye and in the development of career ophthalmic investigators. It has seen, and perhaps been in a small way responsible for, a change in attitude toward research from that of an indulgence to be tolerated as long as it was not expensive to an indispensable and somewhat costly part of a teaching hospital.

The alliance of the Howe Laboratory with the Infirmary has been happy and productive. Providing the quarters in accordance with the original agreement (a sort of nuptial vow) the Infirmary administration has been most cooperative in making available facilities within the limitations of its other obligations. While a laboratory of twice the size of the new quarters could profitably be used, research is after all only one of the aspects of medical care. It would probably be as unwise to permit the unbridled expansion of research at the Infirmary as it would be to repress it arbitrarily. In the opinion of most of us, the Howe Laboratory has comprised a research division properly commensurate in size with the other activities of the hospital. The new quarters, acquired and maintained at a considerable expense for the Infirmary, and staffed by the Howe Laboratory, symbolize the mutual dedication of both to research in ophthalmology. The most reliable prognostication for the future is the record of the past. The environment is certainly favorable and as one who is thoroughly familiar with the staff and esprit de corps I cannot help but be enthusiastically optimistic for the future.

Research Activities

Glaucoma

Keynote of the glaucoma research program at the Howe Laboratory has been close coordination of clinical and experimental work. Study of patients and experimental work have proceeded in adjoining quarters. In one room, special examinations have been made on patients to determine how their intraocular pressure is influenced by rate of secretion of fluid into the eye and by freedom of drainage of fluid out of the eye. In the adjoining laboratory, eyes which have been bequeathed for investigative purposes have been studied to determine how their anatomic, physiologic and biochemical properties may affect control of intraocular pressure. Concurrently, investigations have been carried out on the eyes of animals to help in elucidating normal mechanisms of pressure control. Presumably the studies which are most significant with respect to glaucoma are those performed on human eyes, since glaucoma is a disease of man and does not affect animals in comparable manner.

To perform the desired studies on patients, and on enucleated eyes and on animals, it has been necessary to develop and apply special methods of investigation. For evaluation of secretion and flow of fluid in the eyes of patients the procedure known as tonography has been developed. This is based on electronic recording of intraocular pressure, utilizing equipment similar to that employed for electro-cardiography to provide a recording on a paper strip. For measurements on enucleated eyes and on animal eyes, techniques have been borrowed from aircraft and hydraulic engineering. Electronic strain gages such as are employed to measure forces in aircraft have been utilized in research on glaucoma to provide sensitive measures of intraocular pressure and volume.

The previous clinical investigations carried out with financial assistance from the United States Public Health Service have utilized these methods and have helped establish that the abnormally high intraocular pressure which is characteristic of glaucoma is the consequence of an obstruction to the escape of fluid from the eye rather than the result of a secretion of fluid into the eye at an abnormally high rate. Having made this distinction, attention has been directed to the possible nature and causes of obstruction to outflow. In this way earlier diagnosis and better recognition of different

types of glaucoma has been possible. In one special type it has become apparent that early cure may be achieved by surgical relief of a mechanical blockage of the outflow channels, which in certain eyes is caused by the iris. In other varieties of glaucoma where the cause of obstruction is less evident, studies of secretion and flow of intraocular fluid have led to discovery of the beneficial action of a new drug, Diamox. Substantial advances have been made, but, despite this, many complex problems remain. It is unfortunate that the form of glaucoma which causes most of the blindness is still the least understood.

Current work is a continuation of the clinical and experimental studies reviewed above. That portion of the program which is mainly clinical continues to receive its support from the Institute of Neurological Diseases and Blindness, of the National Institutes of Health, United States Public Health Service, while the experimental portion has become largely dependent upon the Alfred P. Sloan Foundation.

Our recent experimental work has been directed toward establishing the nature of the resistance to outflow of fluid from the eye, which has such critical influence in glaucoma, and to allied problems of regulation of intraocular pressure.

The relationship between pressure, volume and rate of outflow of aqueous humor from enucleated human eyes and the eyes of living rabbits have been evaluated by means of the electronic strain-gage apparatus for purposes of comparison with values previously obtained in patients by tonography. The average outflow from normal human eyes within 24 hours after enucleation was 0.287 microliter per minute per mm. mercury intraocular pressure (50 eyes) at 37° C, compared with an average in vivo of 0.252 microliter per minute per mm. pressure (171 eyes). It was concluded that most of the resistance to outflow normally present in vivo persists after enucleation, and that therefore a stable structure rather than some effect of the general circulatory or nervous system is responsible for the resistance.

It was found by similar comparisons that the abnormal obstruction to outflow which is caused by synechias and newformed vascular tissue in so-called hemorrhagic glaucoma is likewise persistent after enucleation, independent of nervous or circulatory influence. (In other types of glaucoma yet to be studied the condition may of course be quite different.)

Efforts to identify the anatomic site of the normal resistance to outflow of intraocular fluid were made by measurement and dissection of enucleated human eyes. It was found that the external two-thirds of the perilimbal sclera, with its included portions of the outflow channels, could be removed without appreciably increasing the facility of outflow. On the other hand, when the trabecular meshwork in the angle of the anterior chamber of the eye was removed by curetting over a quarter to a third of the circumference, somewhat variable results were obtained. In 12 out of 19 eyes the resistance to outflow was not altered by this procedure, but in 6 eyes a definite decrease in resistance resulted. Gonioscopic examination and microscopic study of histologic sections of these eyes confirmed that the trabecular meshwork had been removed as intended, but in addition there was found to have been some variable inadvertent damage to the adjacent outer wall of Schlemm's canal and to the collector channels. A tentative conclusion was that the trabecular meshwork itself probably offers little resistance to outflow, but that considerable resistance may be encountered in the collector channels. This deserves considerably more investigation, because knowledge of the site and nature of this resistance would be most helpful to elucidation of causes of glaucoma and understanding of the mode of action of drugs which lower the intraocular pressure in glaucoma.

Although, as noted in previous Reports, the outflow in the enucleated normal eye was approximately the same as that found during life, Dr. Rife has found that raising the intraocular pressure artificially in the living rabbit induced responses which tended over a limited range to keep the pressure constant. These responses were not found in enucleated eyes. Experiments are therefore being set up to test the possibility that a homeostatic suppression of aqueous humor formation exists in the rabbit eye. It is not known whether there is a comparable response in the human eye.

In the course of experiments on intraocular pressure regulating mechanisms it has become apparent that the rigidity of the sclera may be less constant than has previously been thought. It is evident that careful reevaluation of the physical properties of the globe would be desirable for improving accuracy of tonometry and tonography.

Lens and Corneal Metabolism

In last year's Report it was noted that glucose metabolism in the lens had been found to differ significantly from that of most other tissues in the body. Whereas most tissues degrade glucose first to lactic acid and thence to carbon dioxide and water, the lens does not have an active mechanism to oxidize the lactic acid formed. To compensate partially for this deficiency it has available a different sequence of reactions called the direct oxidation cycle in which carbon dioxide is split off from the glucose moiety directly. While this direct oxidative cycle is utilized to some extent by many tissues (especially plants), the lens of the eye is unique in depending on it for most of the carbon dioxide produced from glucose. This raises interesting questions, of a biological nature, as to why the lens finds this method particularly serviceable. It also raises the impelling clinical possibility that cataract formation may be linked to this peculiarity of metabolism. Because of their bearing on radiation cataract, these studies are being supported in considerable measure by the Atomic Energy Commission.

Insofar as the peculiarities of the lens metabolism may be due to the absence of a blood supply, it was of considerable interest to subject the cornea to a similar scrutiny since much of the cornea is also devoid of blood vessels. However, the cornea does have direct contact with oxygen through the atmosphere and is known to depend on this for maintenance of transparency. Hence the situation is not entirely analogous. It was not predicted therefore, but nevertheless not surprising, to find that the cornea had significant quantities of the enzymes of the direct oxidative cycle and has therefore metabolic activities which are qualitatively similar to those of the lens. It was while working with the corneal epithelium that a method was developed for estimating the relative extent of glucose degradation by direct oxidation and by the conventional glycolytic pathway. It was also shown in the corneal epithelium that the oxidative enzymes of the direct oxidative cycle were inhibited at very low concentrations of tetracaine, nupercaine, and benoxinate.

Another approach to the elucidation of the cataractous processes is through the study of protein turnover in the lens. Some years ago Dr. Kinsey, in this Laboratory, was able to demonstrate that lens proteins were in a dynamic state, con-

tinually undergoing breakdown and resynthesis. From the rate of incorporation of radioactive glycine into lens protein, it was found that 2½–5% of the protein was turned over each day. Consistent with this fairly active turnover is our finding that various peptidases are present in the lens. These enzymes were demonstrated by their ability to split a number of dipeptides and tripeptides but it is assumed that they also participate in the synthesis of these peptides. For the study of these changes in proteins in the lens we have acquired for the Laboratory some of the equipment for electrophoresis and chromatography. It is hoped to report in a subsequent year a reasonably thorough and penetrating study of lens proteins.

Fat Formation

The experimental production of fat by corneal cells, which was first demonstrated in the Howe Laboratory a few years ago, continues to be one of our major preoccupations. While fat formation is being studied primarily as a biologic phenomenon, the results of the investigation give promise of having particular significance in the fields of atheroma formation, fatty degeneration, and lipidosis corneae. These investigations are being supported by the American and Massachusetts Heart Associations. The use of eye tissue for this study has provided an unusual approach to a general problem and has turned up some unexpected and exciting leads. Thus, it has been found that aberrant lipogenesis or fat formation by non-adipose tissue, depends on the presence of certain unsaturated fatty acids and on a co-factor in serum. Studies of the past year, and continuing at present, have been directed chiefly toward identification of the fat formed, the responsible factor in serum, and the comparative ability of tissues, other than that of the cornea, to form fat. None of these have been established sufficiently to warrant publication at present. To one not familiar with the details, progress may seem slow but the number of experiments necessary to establish one single fact, the number of checks and re-checks necessary to test a theory, and the necessarily inefficient means of obtaining supplies, equipment, and support can be appreciated only by one who is actively engaged in the research. The fact is, however, that a mass of solid information is being obtained on aberrant fat formation which will, almost certainly, have wide implications.

Incidental to the foregoing have been studies, by investigators temporarily attached to the Laboratory, on lipogenesis in corneal transplants, susceptibility of lipogenesis to gamma irradiation, and the spontaneous occurrence of sudanophilia in the cornea. None of these investigations are completed as yet.

Toxicology

A long-term project supported by the Public Health Service concerns mechanisms of corneal injury by chemicals with the ultimate objective of improving treatment of these injuries. Early in this investigation on alkali burns an interest was developed in the binding of ions by the cornea. It was found that cations were bound by the corneal stroma both at alkaline reaction and at neutrality. The amount bound increased steeply in the same range of alkalinity in which injury to the cornea in rabbit eyes became severe. There have been indications that as a consequence of this reaction some of the mucoprotein of the cornea is split loose. This secondary reaction at high pH has not yet proved reversible, although the interaction of foreign cations with the cornea may be reversed. In the case of interaction of cations with the corneal stroma at neutrality the circumstances seem to be more favorable from the standpoint of treatment. It has become apparent that at neutrality there is some physiologic interaction of charged groups in the tissue with the soluble ions which are normally present. The binding of a large series of cations, mostly metals, has been examined and it is found that the amount bound does not vary from substance to substance nearly as much as does the tenacity of the binding. Some cations are found to be loosely bound, while others are held much more firmly. When the cornea is exposed to mixtures of cations for which it has different affinities, the cations compete for reaction with the cornea and those with high affinity become bound to the exclusion of those having low affinity. Interestingly, in a large series of metals those which exhibit high affinity for the cornea are found to be the ones which are toxic, causing opacification and scarring, whereas those having relatively low affinity are innocuous. Furthermore, those cations which exhibit high affinity cause a change in the physical properties of the cornea which might be considered a denaturation of its structural components. Exposure to these substances inhibits the swelling which normally occurs when

pieces of cornea are placed in water. At the same time, certain of these strongly bound toxic metals greatly reduce the extractibility of corneal mucoproteins. Among the most interesting substances showing these properties are beryllium and the so-called rare earth metals. While considerable remains to be learned about the nature of the reaction of these substances with the cornea and the manner in which they alter the physical and vital properties of this tissue, it has been most encouraging to find that in certain instances the initial reaction between metal and cornea is reversible, and injury to the cornea may be significantly alleviated by appropriate treatment. Not only may the swelling properties of the cornea and the solubility of the mucoprotein be regained, but in the living rabbit the degree of injury may be much reduced. These results have been most satisfactorily achieved in the case of the rare earth metals by means of treatment with a solution of ethylenediamine tetra-acetate. (This same substance was previously found to be effective in the treatment of superficial calcific opacities of the cornea from lime burns or in band keratopathy.) However interesting and encouraging they may be, the practical significance of these findings is slight at the present time. Injury of the cornea by many of the substances under study is rarely encountered clinically or in industry. The value in the discovery of these phenomena presumably lies in the knowledge which has been gained and which may be applied to solution of other problems of ophthalmic toxicology.

Miscellaneous

Collaboration with other parts of the medical and scientific community is a continued source of pleasure and profit. The informal contact which the Howe Laboratory maintains with the Division of Neurology has been especially productive of specific accomplishments. A fascinating series of neuroanatomic specimens have been prepared and photographed. These form the basis of a course in ophthalmic neuroanatomy which is being given currently. Some examples were exhibited at the recent Convention of the Teaching Institute. A series of patients with the peculiar neuro-ophthalmic entity known as Spasm of the Near Reflex has been studied with the aim of establishing the diagnostic criteria and therapeutic implications of the condition. Finally, one of the less direct but nonetheless real fruits of the collaboration between the Laboratory

and neurologic interests was the revision of the textbook "Neurology of the Ocular Motor System" which has been out of print, and out of date, for several years past.

Opportunity has presented itself in the past year to study, and possibly make a small contribution to, two systemic diseases with ophthalmic manifestations. They are periarteritis nodosa and cystinosis.

Four patients with periarteritis nodosa or an allied entity known as Wegener's granulomatosis were found to have a characteristic marginal keratitis and necrotizing scleritis. These four cases studied in the Laboratory together with four cases culled from the literature, suggest an ocular syndrome that is characteristic of this disease.

The other systemic condition, cystinosis, which we have had occasion to study was based on five cases referred to us by the Departments of Pediatrics at the Massachusetts General Hospital and the Children's Medical Center. The condition is based on a defective utilization of amino acids with consequent precipitation in the tissue of the relatively insoluble cystine. It has severe general repercussions (renal dwarfism, uremia, and shock) so that its early recognition and treatment is of major, and often life-saving, importance. Its ophthalmic manifestation, recognized only during the past 15 years, consists in the occurrence of fine crystals in the cornea and conjunctiva. The conjoint activity of various members in the Howe Laboratory have resulted in a comprehensive report on the largest group of such cases that has been studied ophthalmologically. Especially informative were the chromatographic identification of the conjunctival crystals as cystine. Although the results of this study cannot be said to have accomplished much more than confirm the observations and speculations of others, they have indicated some of the pathognomonic features of the ocular manifestations of the disease and secured photographic records that should be of great benefit for others who do not have the opportunity to see this rare disease.

Cystinosis in the adult has never been unequivocally proved. It was, therefore, of great interest to us that an otherwise normal adult man, referred to the Laboratory by Dr. Linus Sheehan, had crystals in his cornea and conjunctiva that appear to be identical with those of cystinosis in childhood. Identification of the crystals is being carried out at present

but preliminary observations, based on staining reactions, solubility, and chromatography, are compatible with their being cystine.

The possibly allergic nature of some ocular diseases, especially uveitis, has often prompted the experimental study of ocular inflammation induced by injecting antigen into the eye. The Howe Laboratory has, in a small way, been able to participate in what is believed to be the first attempt to quantitate an allergic reaction in the eye. The experiments, conceived and conducted by Drs. Byron Waksman and Sunny Bullington, consisted in the experimental production of an Arthus reaction wherein known amounts of antigen and antibody administered by different routes are caused to react within the eye. Although the resulting reaction in the rabbit eye is quantitatively similar to that in the rabbit skin, two surprising phenomena were observed. First, the eyes showed a more intense reaction when the antigen, injected into the vitreous, is given two days prior to the intravenous injection of the antibody than when given immediately. Secondly, although guinea pigs show an Arthus reaction in the skin similar to that of rabbits, no comparable reaction is induced in the eye when the antigen is injected intraocularly and the antibody intravenously. These phenomena are unexplained.

The testing of vision in infants is often important but frustratingly difficult. The opticokinetic response has been used with varying success in the past and the Howe Laboratory has had, during the past year, the privilege of assisting Dr. John Gorman to develop an apparatus that may be more practicable than any heretofore devised. It is hoped that the apparatus will be able to indicate an infant's vision in terms comparable to the standard acuity criteria of adults.

Research of a different nature is the development of ocular photography. Striking success was achieved this past year in taking three dimensional photographs of the angle of the anterior chamber, so-called goniophotography. But what is more exciting is the development of a new type of fundus camera since previous cameras for this purpose have major disadvantages. An experimental fundus camera has now been made which uses the direct ophthalmoscopic method as opposed to the indirect, and takes pictures of a comparable area, but

has considerably greater depth of field and an improved method of focussing. In addition it takes simultaneous stereoscopic pairs of photographs.

Inasmuch as these Annual Reports are intended to provide some historical continuity in the activities and accomplishments of the Howe Laboratory, it is necessary to list the specific awards and citations which have been received for research by its staff members. Previous Reports have been incomplete in this regard and have been criticized for it. For the record, therefore, it may be stated that in the previous years covered by these Reports members of the staff have received the Warren Triennial Prize of the Massachusetts General Hospital (1943), the Proctor Medal awarded by the Association for Research in Ophthalmology (1954), the Annual Prize of the New England Ophthalmological Society (1950 and 1953) and several Blue Ribbon awards for exhibits at meetings of the American Medical Association and the American Academy of Ophthalmology and Otolaryngology. In addition members of the Laboratory staff were again awarded this past year the Annual Prize of the New England Ophthalmological Society and also the Knapp Medal of the Section of Ophthalmology of the American Medical Association. While the listing of these citations may unfortunately seem ostentatious, it is properly part of the historical record of the Laboratory and may serve as evidence of the respect that the Laboratory is held by its professional colleagues.

Service Activities

For the purposes of this Report research and service functions are considered separately. In fact, however, no such sharp distinction exists. In a laboratory which is devoted to the integration of the basic sciences with clinical practice, give and take is mutual. Just as it is advantageous for a hospital to have a research department in its midst, so is it essential to a laboratory such as ours to have clinical facilities and cooperative clinicians nearby.

The pathology department of the Eye Service has been operated jointly in the past two years by the Infirmary and the Howe Laboratory. Dr. Taylor Smith, now Associate Pathologist, has devoted practically full time to the operation

of the department and has progressively relieved Dr. Cogan of the responsibilities involved. At present he is assisted by Dr. Frank Milam, a Public Health Service Fellow, and by the resident staff. Studies requiring special stains or preparations are carried out by Dr. Kuwabara. A cross reference system, similar to that used in the Howe Laboratory, has been set up for the filing and cross referencing of cases. The weekly pathology conferences which are operated by, and for, the house officers have proved most valuable as a teaching medium. Here all the specimens of the preceding week are reviewed with Dr. Verhoeff and other interested persons in and out of the Infirmary. Emphasis is put on the correlation of the clinical and pathological findings.

The active research on glaucoma in recent years and the close coordination of the clinical and experimental work has been progressively aggravating the space situation. With the development of tonography as a diagnostic tool an increasing number of patients have been referred to the Laboratory not only for investigative purposes but for clinical assistance. Since it seemed that this type of service would more appropriately be a function of the hospital rather than of the laboratory, the Massachusetts Eye and Ear Infirmary was urged to make provision for a glaucoma consultation service, and this it has done. A room has been provided near the Out-patient Eye Clinic for special clinical study of glaucomatous patients whenever this is requested by the eye clinic or private ophthalmologist. This consultation service has been organized by Doctor Trotter; each ophthalmic resident in rotation is to spend a three months' training period on this Service. Funds from the Laboratory have provided some support to the Service during its inception, but it is hoped that the Service may soon become self-supporting and will free these funds for further research. A liaison engendered by common interests is expected to continue to connect the new consultation service and the Laboratory. It is to be expected that with improved facilities and the welfare of the patient ensured, there may be an expansion of both clinical and experimental research in glaucoma.

The first product of this new opportunity for residents in training to make special study of glaucoma has been an investigation of the influence of a new mydriatic drug (Cyclogil) on

the intraocular pressure. This study is being carried out by Dr. Sachs, first resident on the new Consultation Service.

The Laboratory and the Glaucoma Consultation Service have made a cooperative study on the calibration of Schiotz tonometers, carrying out comparative measurements on patients and on enucleated human eyes. The aim of this study is eventual improvement in the accuracy of measurement of intraocular pressure and attainment of greater precision for tonography and for diagnosis of glaucoma.

During the past six years stereoscopic photographs have been taken of interesting cases which have come to the Howe Laboratory from various sources. More than 6,000 of these slides are now filed in Dr. Donaldson's laboratory according to the clinical condition represented. Of these, some 300 have been especially selected as being particularly valuable for post-graduate teaching purposes. These slides along with abstracts of the histories and discussion of the cases are in a separate group available to the residents and visiting ophthalmologists. In addition, a number of ophthalmic operative procedures have been photographed and these have been found to be of considerable value to the resident staff.

During the past year the neuroanatomy portion of the post-graduate course was completely revised with the addition of new dissections shown by stereoscopic slides. The text was rewritten and because of the demand for these sets of slides they are now available at cost to other institutions along with the text material in book form and a stereoscopic viewer.

Without prior intent or plan, an arrangement has developed whereby incoming house officers spend several months in the Laboratory before their residency. This has been a haphazard arrangement initiated, for the most part, by the men themselves on a volunteer basis. The success of the arrangement has been attested to by the specific accomplishments during this period and by their subsequent contacts during the resident period. Since the financial status of men in this category is notably precarious, ways are being explored that might support such short-term training periods.

The prime teaching responsibilities of a formal nature have been in the Harvard Postgraduate Course. Members of the Laboratory staff have taught particularly in the fields

of physiology, bio-chemistry, pathology, and ophthalmic neuroanatomy. Some have also participated in the Study Council Course and in many other less formal ways. At the request of the National Institute of Health a course in Neuro-ophthalmology is being prepared for presentation this spring at the Clinical Center of the Institute.

Provision of teaching material to the Infirmary staff and others has been a self-imposed function of the Laboratory for some time, but it was not formalized until this year. We have now deposited in the Howe Library, under the custodianship of the librarian, a catalogued collection of photographs illustrating various aspects of ocular disease. These are standard sized slides, instead of the anomalous-sized stereophotographs previously available, and will fit into a standard projector. The new library will also house a permanent collection of stereophotographs for on-the-spot viewing.

The Howe Library of Ophthalmology and the Howe Laboratory have grown together. Situated close together they have enjoyed mutual contacts and interchange of functions. Mr. Charles Snyder, the librarian, has been in effect, if not in name, a staff member of the Laboratory. It is with major misgivings, therefore, that the Library and Laboratory must now be situated on separate floors in the new quarters. There seemed to be no alternative, however. The expansion of the Library, now serving the Ear, Nose and Throat Services as well as the Eye Service, and the expansion of the Laboratory, necessitated their being placed on separate floors. Progress is not always pure gain.

Conclusions

The task of writing an Annual Report, discouraging as may be the forced contemplations of one's own limitations, is nevertheless a pleasurable experience in the end. It underscores the privileged position in which a few persons find themselves in being able to devote their lives to such a worthy cause as ophthalmic research. It also brings into focus the innate charity of a large number of people who, not participating directly in the investigations themselves, have given unselfishly to the end that these investigations may be furthered. It is to the benefactions of these individuals — their financial support, their invaluable counsel, and their solid loyalty — that we are perennially in debt.

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Mr. J. M. Ulmer
Mr. Sam White

For training purposes:
For studies on tonography and toxicology of the eye:
For studies of eyes in identical and fraternal twins:

U. S. Public Health Service

For studies on radiation cataracts:
For studies on metabolism of the ocular lens:

Atomic Energy Commission

For studies on intraocular fluids and glaucoma:

The Alfred P. Sloan Foundation

For studies on fat metabolism in the cornea and aging processes as reflected in the cornea:

The Massachusetts Heart Association
The American Heart Association

DAVID G. COGAN, M.D.
Director

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TROTTER, R. R.

with Chandler, P. A. Angle-closure glaucoma; subacute types. A.M.A. Arch. Ophth. 53:305–317, March, 1955.
(see also Grant, W. M.)

LECTURES

COGAN, D. G.

The eye in general medical diseases. Veterans Administration, in Boston, Massachusetts, March 22, 1955.

Eye pathology. Harvard Medical School, Department of Pathology, in Boston, Massachusetts, March 28, 1955.

Ocular fundus. Postgraduate Course in Cardiology, Massachusetts General Hospital, in Boston, Massachusetts, April 5, 1955.

House Officer Lectures, Massachusetts Eye and Ear Infirmary.

Eye pathology. April 7, 1955.
Neuro-ophthalmology. October 13, 1955.

Eye pathology. House Officers in Pathology at the Massachusetts General Hospital, in Boston, Massachusetts, November 18, 1955.

COGAN, D. G. (*continued*)

with Kuwabara, T. Further studies on corneal lipogenesis. Presented by Dr. Cogan at the Eastern Section meeting of the Association for Research in Ophthalmology, in Boston, Massachusetts, April 25, 1955.

Paralimbal keratitis and scleritis occurring as part of a fatal systemic disease. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 26, 1955.

Ocular motor dysmetria, flutter, and opsoclonus. Fellows Society of Montreal Neurologic Institute, in Montreal, Canada, May 30, 1955.

Palsies of conjugate lateral gaze. Montreal Ophthalmological Society in Montreal, Canada, May 30, 1955.

Corneoscleral lesions in periarteritis nodosa and Wegener's granulomatosis. American Ophthalmological Society, in White Sulphur Springs, West Virginia, June 4, 1955.

with Kuwabara, T. Aberrant lipogenesis in the corneal explant. Presented by Dr. Cogan as part of Symposium on Lipoproteins and Atherosclerosis, Harvard Medical Society, in Boston, Massachusetts, December 13, 1955.

DONALDSON, D. D.

A review of experimental and clinical radiation cataracts. Atomic Energy Commission Industrial Physicians Meeting, in Rochester, New York, January 19, 1955.

Corneal dystrophies. Buffalo Ophthalmological Club, in Buffalo, New York, March 10, 1955.

Instrumentation in ophthalmology. The Optical Society of America, in New York City, New York, April 7, 1955.

A heretofore undescribed heredo-congenital corneal dystrophy. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 27, 1955.

Anterior segment diseases in pediatrics. Pediatrics Staff, Massachusetts General Hospital, in Boston, Massachusetts, May 12, 1955.

Close-up stereophotography. Photographic Society of America Meeting, in Boston, Massachusetts, October 7, 1955.

Stereophotography in the medical field. Teaching Institute of the Association of American Medical Colleges, in Swampscott, Massachusetts, October 19, 1955 (Exhibit).

GRANT, W. M.

Pathology of glaucoma. Lecture to House Officers, Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 5, 1955.

Outflow measurements in enucleated eyes. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 26, 1955.

GRANT, W. M. (*continued*)

Tonography in chronic glaucoma. Symposium on Glaucoma, New York Medical Society, in Buffalo, New York, May 12, 1955.

with Kern, H. L. Corneal bonding of rare earths and other cations. Presented by Dr. Grant at the Conference on Rare Earths in Biochemical and Medical Research. Oak Ridge Institute of Nuclear Studies, at Oak Ridge, Tennessee, October 28, 1955.

Participated in the Josiah Macy Jr. Foundation Conference Program: Symposium on Glaucoma, in Princeton, New Jersey, December 5, 6, and 7, 1955.

Ophthalmic toxicology. Lecture to House Officers, Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, December 15, 1955.

(see also Kern, H. L.)

KERN, H. L.

with Grant, W. M. Binding of cations by the corneal stroma. Presented by Dr. Kern at the Eastern Section Meeting of the Association for Research in Ophthalmology, in Boston, Massachusetts, April 25, 1955.

(see also Grant, W. M.)

KINOSHITA, J. H.

Hexose monophosphate shunt mechanism. Department of Biochemistry Seminar, Harvard Medical School, in Boston, Massachusetts, February 28, 1955.

Carbohydrate metabolism of lens. Conference on Radiation Cataracts, National Academy of Sciences, National Research Council, in Washington D. C., March 18, 1955.

Carbohydrate metabolism of ocular tissue. Eastern Section Meeting of the Association for Research in Ophthalmology, in Boston, Massachusetts, April 25, 1955.

KUWABARA, T.

(see Cogan, D. G.)

TROTTER, R. R.

Gonioscopy. American College of Surgeons (New Jersey Ophthalmological Group), January 15, 1955.

Glaucoma. Massachusetts State Nurses Association, February 3, 1955.

Observations on the influences of new drugs on intraocular pressure. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 26, 1955.

Recent developments in glaucoma. Boston City Hospital, Eye and Ear Alumni Meeting, April 27, 1955.

Glaucoma. Series of lectures to student nurses from Radcliffe and Simmons Colleges at the Massachusetts General Hospital, in Boston, Massachusetts, May 14, 16, 20, 23, 1955.

Long-term Diamox treatment. Section on Ophthalmology, American Medical Association, in Atlantic City, New Jersey, June 8, 1955.

Glaucoma. Series of lectures to graduate nurses at Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, June 15, July 14, October 26, November 15, 1955.

Long-term Diamox treatment. American Academy of Ophthalmology and Otolaryngology, in Chicago, Illinois, October 11, 1955.

Secondary glaucoma. Lecture to House Officers, Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, October 25, 1955.

Glaucoma Consultation Service — its origin and functions. Social Service Department of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, November 17, 1955.

FORM OF BEQUEST

The Howe Laboratory of Ophthalmology is an independent department of the Harvard Medical School and is jointly supported by a restricted endowment of Harvard University and by the Massachusetts Eye and Ear Infirmary.

For the information of those who may wish to contribute to this Laboratory, a form of bequest is here set forth:

I Give and Bequeath to the Howe Laboratory of Ophthalmology .....Dollars to be Applied to the Uses of Said Laboratory.

Such bequests are managed by the Treasurer's Office of Harvard University, and the income is accredited to the Laboratory.